PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor: Guilherme L. INDIG

Serial No.: 09/753,472 Docket No.: 032026:0667

Filed: January 3, 2001 Group Art Unit: 1614

For: **USE OF CRYSTAL VIOLET AS PHOTOCHEMOTHERAPEUTIC AGENT**

DECLARATION UNDER 37 C.F.R. § 1.132 OF GUILHERME L. INDIG

Box Non-Fee Amendment
Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Guilherme L. Indig, state and declare that:

1. I am an Assistant Professor of Pharmacy at the University of Wisconsin-Madison, located in Madison, Wisconsin.

2. I am one of six authors of the paper entitled "EFFECT OF MOLECULAR STRUCTURE ON THE PERFORMANCE OF TRIARYLMETHANE DYES AS THERAPEUTIC AGENTS FOR PHOTOCHEMICAL PURGING OF AUTOLOGOUS BONE MARROW GRAFTS FROM RESIDUAL TUMOR CELLS," published in the Journal of Pharmaceutical Sciences, Vol. 89, No. 1, January 2000. The other authors of the paper are Gregory S. Anderson, Michael G. Nichols, Jeremy A. Bartlett, William S. Mellon and Fritz Sieber.

3. I have read the above-identified application for patent and declare that I am the sole inventor of the subject matter claimed therein.

4. I conceived and directed the research described in the paper described in paragraph 2 above, and I was the lead investigator of the research.

5. The co-authors of the paper described in paragraph 2 above, other than myself, did not make an inventive contribution to the subject matter claimed in the application.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: August 15, 2003 By: Guilherme Luiz Indig

Guilherme L. Indig

THE UNITED

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MINI-REVIEW

RESEARCH ARTICLES

(*continued*)

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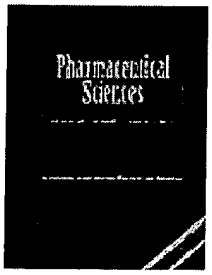

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Research Article

Effect of molecular structure on the performance of triarylmethane dyes as therapeutic agents for photochemical purging of autologous bone marrow grafts from residual tumor cells

Guilherme L. Indig [1 *], Gregory S. Anderson [2], Michael G. Nichols [3], Jeremy A. Bartlett [1], William S. Mellon [1], Fritz Sieber [2 *]

[1]School of Pharmacy, Division of Pharmaceutical Sciences, University of Wisconsin, Madison, WI 53706
[2]Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI 53223
[3]Department of Applied and Engineering Physics, Cornell University, Ithaca, NY 14853
email: Guilherme L. Indig (glindig@facstaff.wisc.edu)

*Correspondence to Guilherme L. Indig, School of Pharmacy, Division of Pharmaceutical Sciences, University of Wisconsin, Madison, WI 53706

*Correspondence to Fritz Sieber, School of Pharmacy, Division of Pharmaceutical Sciences, University of Wisconsin, Madison, WI 53706

Abstract

Extensively conjugated cationic molecules with appropriate structural features naturally accumulate into the mitochondria of living cells, a phenomenon typically more prominent in tumor than in normal cells. Because a variety of tumor cells also retain pertinent cationic structures for longer periods of time compared with normal cells, mitochondrial targeting has been proposed as a selective therapeutic strategy of relevance for both chemotherapy and photochemotherapy of neoplastic diseases. Here we report that the triarylmethane dye crystal violet stains cell mitochondria with efficiency and selectivity, and is a promising candidate for photochemotherapy applications. Crystal violet exhibits pronounced phototoxicity toward L1210 leukemia cells but comparatively small toxic effects toward normal hematopoietic cells (murine granulocyte-macrophage progenitors, CFU-GM). On the basis of a comparative examination of chemical, photochemical, and phototoxic properties of crystal violet and other triarylmethane dyes, we have identified interdependencies between molecular structure, and selective phototoxicity toward tumor cells. These structure-activity relationships represent useful guidelines for the development of novel purging protocols to promote selective elimination of residual tumor cells from autologous bone marrow grafts with minimum toxicity to normal hematopoietic stem cells. © 2000 Wiley-Liss, Inc. and the American Pharmaceutical Association J Pharm Sci 89: 88-99, 2000

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February 13, 2004

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor: Guilherme L. INDIG

Docket No: 032026:0769

Serial No: 10/751, 302

FAX: 608.258.4258

Field: December 31, 2003

For: **USE OF CRYSTAL VIOLET AS PHOTOCHEMOTHERAPEUTIC AGENT**

DECLERATION UNDER 37 C.F.R. § 1.132 OF S.G. PANDALAI

Mail Stop NON-FEE AMENDMENT
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

I.S.G. Pandalai, state and declare that:

1. I am the Managing Editor of Transworld Research Network, publishers of the book, *Recent Research and Development in Pure & Applied Chemistry*, Vol.3(1999). An article entitled "Mechanisms of Action of Cationic Dyes in Photodynamic Therapy of Tumors," authored by Guilherme L. Indig appears on pages 9 through 19 of the book.

2. Although the book *Recent Research and Development in Pure & Applied Chemistry*, Vol.3 (1999) bears a publication year of 1999, it was actually first published in March of 2000.

3. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 13th February, 2004

By: S.G. Pandalai

***This declaration is submitted as per the request of Dr. Michelle Manning**

FEDERAL SECURITY AGENCY
Public Health Service

AN INDEX OF TUMOR CHEMOTHERAPY

A tabulated compilation of data from the literature on clinical and experimental investigations

"If no use is made of the labors of past ages, the world must remain always in the infancy of knowledge.—" Cicero

JEROME D. GOLDBERG
EXAMINER
GROUP ART UNIT 125

By HELEN M. DYER, Biochemist
National Cancer Institute
National Institutes of Health

NOTES TO TABULATED INDEX

Column 1 - No.--The *numbers* correspond to the numbers that follow the names of the agents in the alphabetical index.

Column 2 - Agent--No attempt has been made to use a consistent system of nomenclature for the chemical agents. Most frequently, the terminology employed in the original papers has been retained in the classified index. The alphabetical index of agents contains cross references between some of the names used in the classified index and the names of the agents according to the nomenclature of *Chemical Abstracts*.

Optional names for some of the agents are given in parentheses and are in italics.

Trade names of agents, when used, are found within parentheses in quotation marks.

Agents used for *supplementary treatment* are also included in parentheses but are not italicized. They are included in the alphabetical index.

To save space *chemical symbols* of chemical *elements* have been used for supplementary therapeutic agents when no special emphasis was made of the specific substances that contained the elements. Such symbols are not meant to indicate that elementary ions were administered as such. *Chemical formulas* of *compounds* have been used, where feasible, for simple inorganic supplementary agents.

Gas treatment refers to supplementary exposure of the tumor-bearing host to mixtures of carbon dioxide and oxygen.

Column 6 - Dosage--*Dosage* is expressed as *milligrams* except where otherwise indicated.

Column 7 - Number of Treatments--*Numbers in parentheses* following daily, weekly, etc. refer to *total number* of treatments.

Columns 9 and 10 - Effect Claimed--In these columns the *numbers* refer to the *numbers of hosts* showing the effect.

Column 9 - Effect on Tumor--The symbols and abbreviations for this column are as follows:

(±) .... growth of tumor inhibited
(+) .... diminution in size of tumor
C ..... cure
hemor. . hemmorhage in tumor
nec. ... necrosis in tumor
R ..... complete regression of tumor
stim. .. stimulation of tumor growth
temp. .. temporary

Column 10 - Effect on Host --The symbols and abbreviations for this column are as follows:

(±) .... slight subjective improvement in host and/or diminution of pain
(+) .... significant subjective improvement
S>..... survival of treated animals for longer period of time than controls
Tox. ... agent said to have toxic effects upon host

Column 11 - Reference Number--The *reference number* corresponds to the number found to the left of the reference in the bibliography.

ABBREVIATIONS

ac. ..... acute
adcar. ..... adenocarcinoma
aden. ..... adenoma
amt. ..... amount
autol. ..... autologous
Bash. ..... Bashford
B. P. ..... Brown-Pearce
Buf. ..... Buffalo
bzp ..... benzpyrene
can. ..... cancer
car. ..... carcinoma
ca ..... cholanthrene
chond. ..... chondroma
ch. ..... chronic
Cr. ..... Crocker
dbza ..... dibenzanthracene
deriv. ..... derivative
dil. ..... dilute
div. ..... divided
dmaabz ..... dimethylaminoazobenzene

dmbza 7,10-dimethyl-1,2-benzacridine
Ehr. ..... Ehrlich
elect. ..... electrically
epithel. ..... epithelioma
= ..... equals
esoph. ..... esophagus
estro. ..... estrogen
ext. ..... external
Flex. ..... Flexner
F. J. ..... Flexner-Jobling
Fuj. ..... Fujiwawa
Gal. ..... Galliera
gast. ..... gastric
gm ..... gram
> ..... greater than
H. P. ..... Harding-Passey
heterol. ..... heterologous
Hodg. dis. ..... Hodgkin's disease
homol. ..... homologous
hrly. ..... hourly
HCl ..... hydrochloride
ic ..... intracardial
id ..... intradermal
ig ..... intragastric (by stomach tube)
im ..... intramuscular
ind. ..... induced
ind. (tar) ..... induced by tar, etc.
inj. ..... injection or injected
int. ..... interval
ip ..... intraperitoneal
irrad. ..... irradiation
it ..... intratumoral
iv ..... intravenous
iv(sc) ..... intravenous, occasionally subcutaneous
Jen. ..... Jensen
K ..... kilogram
< ..... less than
L.D. ..... lethal dose
leuk. ..... leukemia
leukos. ..... leukosis
loc. ..... local application
lym. ..... lymphatic
lymgran. ..... lymphogranuloma
lymph. ..... lymphoma
lymsar. ..... lymphosarcoma
ma. ..... mammary
mc ..... millicurie
mca ..... methylcholanthrene
Mch. u ..... Mache unit
mel. ..... melanoma
melsar. ..... melanosarcoma
metas. ..... metastasis or metastasizing
m. fung. ..... mycosis fungoides
mg ..... milligram
min. ..... minim
misc. ..... miscellaneous
ml ..... milliliter
m.u ..... mouse unit
mult. ..... multiple
mye. ..... myelogenous
myel. ..... myeloma
osteosar. ..... osteosarcoma
ovar. ..... ovarian
pap. ..... papilloma
Phila. ..... Philadelphia
± ..... with or without
polycy. ..... polycythemia vera
prep. ..... preparation or prepared
Put. ..... Putnoky
r ..... Röntgen
sar. ..... sarcoma
sat. ..... saturated solution
sc ..... subcutaneous
sol. ..... solution
sp. ..... spontaneous
suppl. ..... supplementary
surg. ..... surgery
Teut. ..... Teutschländer
T.D. ..... tolerated dose
tr. ..... transplant, transplantation or transplanted
tr. tar-ind. ..... transplanted tar-induced, etc.
treat. ..... treatment
vag. ..... vaginal
tum. ..... tumor
u ..... unit
ulc. ..... ulcerated
uter. ..... uterus, uterine
u.v. ..... ultraviolet
Wal. ..... Walker

Colons have been used to avoid repetition of words where several types of tumors have been employed in a test. Thus, *Tr.: car., sar.* indicates *transplanted carcinoma* and *transplanted sarcoma*. The same is true, when for other reasons, colons or semicolons are used between car. and sar. following the *Tr.:* Except where man is the host (in which case all the tumors are spontaneous) *tr.:*, when followed by a colon carries over until *ind.* or *sp.* appear. The same is true for *ind.:* or sp.:.

Commas have been used to separate varied experimental conditions in a single test (as different types of tumors and/or kinds of hosts, dosage, routes of administration) where no significant difference was reported in the therapeutic effect of the agent relating specifically to the varied conditions.

Semicolons have been used to relate varied experimental conditions in different columns where the conditions were considered to be of significance.

Example 1: Under agent No. 1 in the table both spontaneous and transplanted carcinomas of the mouse showed an inhibiting effect of the agent. When administered in the drinking water diminution (+) in the size of tumors and regressions, R, were reported; when administered subcutaneously only an inhibiting effect (+) was reported.

Example 2: Under agent No. 13 no distinction was made in dosage, number of treatments or routes of administration, but the effect on the tumors was reported as negative for the transplanted carcinoma, negative for the transplanted sarcoma, positive for the induced-tar papilloma and negative for the induced-tar carcinoma.

Example 3: Under agent No. 25 the therapeutic effect was the same for spontaneous or transplanted carcinomas of the mouse, for spontaneous carcinomas of the dog and for transplanted sarcomas of the rat, but the agent was more effective (+) when administered intravenously than when given subcutaneously (±).

Sometimes a *semicolon* is found in the supplementary treatment (within parentheses) under agent, when this experimental condition has been shown to have a significant influence on the effect of therapy.

Example 4: Colloidal lead (without; with irradiation), and in the Effect Claimed columns (-); (+) indicates that colloidal lead was found to be ineffective when administered alone but beneficial when given with irradiation.

NO.	AGENT	TYPE OF TUMOR	HOST		THERAPY					REFERENCE	
			SPECIES	NUMBER	DOSAGE	NUMBER OF TREATMENTS	ROUTE	EFFECT CLAIMED: TUMOR (Objective)	EFFECT CLAIMED: HOST (Subjective)	NUMBER	DATE
3475	Trypan red *(C.I. No.438:disazo)*	Car.,breast	Man	1	500;.5%	Repeated	Oral;sc	(-);(+)		952	1905
3476	---- ---- (and cocaine)	Can.:gastric;lym. adcar.	"	2;1	500	"	sc	(?);(+)		1728	1906
3477	" "	Sp.ma.car.	Mouse,Marsh	3	2	16	iv,sc	(-)		1306	1927
3478	" "	Ind.(tar)car.	Mouse	20-50	4	Weekly	iv	(-)		659	1931
3479	" "	Tr.lym.sar.	Mouse,C3H	4	1	10-16	sc	(-)		2140	1946
3480	Unclassified azo dyes (17 samples)	Tr.sar.	Mouse	25 each	.15-.4%	14 days	In food	(-)		1199	1947
3481	Vital new red *("Grübler")*	Tr.car.206	"	19	.5%	8	sc	(-)stim.		1245	1931
3482	Vital red *(C.I. No.456:disazo)*	Sp.ma.car.	Mouse,Marsh	6	2	14-19	iv,sc	(-)		1306	1927
	(2). OTHER MISCELLANEOUS CLASSES: ANTHRAQUINONE;NITRO;NITROSO;QUINOLINE;THIAZOLE DYES.										
3483	Ahco 26-47 *(1,4-diaminoanthraquinone)*	Tr.:car.;sar.	Mouse	25;25	25%	16 days	In food	(+)	Tox.	1199	1947
3484	Alizarin	Sp.ma.car.	Mouse,Marsh	3	.05 ml sat	53	sc	(-)		1306	1927
3485	---- red S *(C.I.No.1034;anthraquinone dye)*	Tr.:car.;sar.	Mouse	3	1	50	iv, sc	(-)		1306	1927
3486	Aniline trichloratum *(As-free)*	Car.,ma.;sar.	Man	4;1	1-4 gm	Repeated	It	(-),(+);(+)	(+),tox.	2059,2060	1891,'92
3487	Anthraquinone dyes *(61 samples)*	Tr.sar.	Mouse	25 each	.15-.4%	14 days	In food	(-)		1199	1947
3488	---- ---- (vat, 57 samples)	" "	"	25 each	.15-.4%	14 days	" "	(-)		1199	1947
3489	----,1,4,5,8-tetramine-(AQD-241)	Tr.:car.;sar.	"	25;25	.15-.4%	14 days	" "	(±);(±)		1199	1947
3490	Isoquinoline red	Tr.car.	"	13	—	—	—	(+), 6C		996	1931
3491	Martin's yellow *(2,4-dinitro-1-naphthol,salt of-)*	" "	"	5	—	—	—	(-)		996	1931
3492	Naphthol green B *(C.I.No.5:nitroso dye)*	Sp.car.	Mouse,Marsh	3	8	33	iv,sc	(-)		1306	1927
3493	" "	Tr.car.	Mouse	—	10	Repeated	sc	(+),2R	Tox.	640	1930
3494	Naphthol yellow *(C.I.No.9:nitroso dye)*	Sp.ma.car.	Mouse,Inbred	1	3	62	iv,sc	(-)		1795	1926
3495	Nitro dyes (4 samples)	Tr.sar.	Mouse	25 each	.15-.4%	14 days	In food	(-)		1199	1947
3496	Nitroso dyes (2 samples)	" "	"	25 each	.15-.4%	14 days	" "	(-)		1199	1947
3497	Primuline *(C.I.No.812:thiazole dye)*	Sp.ma.car.	Mouse,Marsh	3	.2ml sat.	46	sc	(-)		1306	1927
3498	Quinoline dyes (5 samples)	Tr.sar.	Mouse	25 each	.15-.4%	14 days	In food	(-)		1199	1947
3499	Quinoline yellow *(C.I.No.801)*	Sp.ma.car.	Mouse,Marsh	6	20	33-67	iv,sc	(-)		1306	1927
3500	" "	Tr.sar.	Mouse —	6	20	33-67	" "	(-)		1199	1947
3501	Soledon blue *(anthraquinone dye)*	Tr.Wal.car.256	Rat	12-15	25	1	ip	(-)		76	1942
3502	Sulfur dyes (11 samples)	Tr.sar.	Mouse	25 each	.15-.4%	14 days	In food	(-)		1199	1947
3503	Tartrazine *(Buffalo-yellow:C.I.No.640: pyrazolon dye)*	Sp.ma.car.	Mouse,Marsh	3	60	45	iv,sc	(-)		1306	1927
3504	Thiazole dyes (10 samples)	Tr.sar.	Mouse	25 each	.15-.4%	14 days	In food	(-)		1199	1947
3505	Thioaniline dye	Tr.Buf.sar.	Rat	—	—	—	iv,sc	(±)	Tox.	2116	1916
	(3). TRIPHENYL-METHANE DYES										
3506	Alkali blue *(C.I.No.710:similar or identical to isamine blue)*	Sp.ma.car.	Mouse,Marsh	3	.4 ml sat.	27	" "	(-)		1306	1927
3507	Aniline blue	Tr.car.2146	Mouse,MRC	5	.3%	*Ad lib*	In food	(±)		1630	1948
3508	Auramine O *(C.I.No.655:pyoktanin yellow)*	Sp.ma.car.	Mouse,Marsh	3	.4	26	iv,sc	(-)		1306	1927
3509	Biorubin *(C.I.No.678:new fuchsin,iso-rubin)*	" " "	" "	3	.2	39	" "	(-)		1306	1927
3510	Brilliant dianiline blue 6G *(C.I.No.710:isamine blue 6B,8B)*	Ind.(tar)car.	Mouse	30-50	10	Weekly	Iv	(-)		659	1931
3511	Cotton blue *(C.I.No.707:Poirrier's blue)*	Sp.ma.car.	Mouse,Marsh	3	4	14	sc	(-)		1306	1927
3512	Crystal violet *(C.I.No.681:gentian violet, methyl violet)*	Car.;sar.	Man	6;4	2000-3000	21-125	It	(±);(+)	(+)	2060	1892
3513	Crystal violet	Sp.ma.car.	Mouse,Marsh	3	.5	25	iv,sc	(-)		1306	1927
3514	---- ---- (with gas treat.)	Tr.misc.tum.	Mouse	—	.2-.3ml	Repeated	sc	—	Tox.	640	1930

NO.	AGENT	TYPE OF TUMOR	HOST		THERAPY					REFERENCE	
			SPECIES	NUMBER	DOSAGE	NUMBER OF TREATMENTS	ROUTE	EFFECT CLAIMED		NUMBER	DATE
								TUMOR (Objective)	HOST (Subjective)		
3515	Crystal violet	Tr.car.2146	Mouse, MRC	5	.3%	*Ad lib*	In food	(+)	Tox.	1630	1948
3516	---- ---- (B.P.C.)	Tr.car.2146	" "	5	.3%	" "	" "	(+)	"	1630	1948
3517	Dahlia *(C.I.No.679:Hofmann's violet)*	Sp.ma.car.	Mouse	6	.2-1 ml sat.	9-22	iv,sc	(-)		1306	1927
3518	Erioglaucine	" " "	"	3	20	44	" "	(-)		1306	1927
3519	Ethyl violet *(C.I.No.682)*	" " "	"	3	.33	14	" "	(-)		1306	1927
3520	---- ---- *(hexaethyltriaminotriphenyl-carbinol anhydride)*	Tr.:car.;sar.	"	25;25	.2%	14 days	In food	(+);(+)	Tox.	1199	1947
3521	" "										
3522	Fuchsin *(amaranth,dahlia etc.)*	Tr.:car.2146;Cr.sar.180	Mouse, MRC	15;5	.3%;.5%	*Ad lib*	" "	(+);(-)		1630	1948
3523	"	Misc.car.	Man	4	—	Repeated	Local	—	(+)	543	1890-91
3524	"	Epithel.	"	1	—	"	—	(+)	(+)	1343	1891
3525	---- (acid: *rubine S)*	Sp.ma.car.	Mouse, Inbred	3	.3-.4	9-10	iv,sc	(-)		1795	1926
3526	---- (neutral)	" " "	" "	1	17-34	26	" "	(-)		1795	1926
3527	---- (acid)	" " "	" "	1	.5	19	sc	(-)		1795	1926
3528	"	Ind.(tar)car.	Mouse	20-50	40	Weekly	iv	(-)		659	1931
3529	---- (basic: ± heparin)	Tr.Tsunoda sar.	Rat	—	—	Repeated	"	(-)		1776	1934
		Tr.car.2146	Mouse, MRC	5;5;5	1%;.5-1 ml;.3%	1;daily;*ad lib*	With tr.; sc; in food	(+);(-);(-)		1630	1948
3530	Gentian violet (see also crystal violet)	Sp.ma.car.	Mouse, Inbred	3	.5-4	7-13	iv,sc	(-)		1795	1926
3531	Glacier blue	Tr.car.2146	Mouse, MRC	5	.3%	*Ad lib*	In food	(-)		1630	1948
3532	Hofmann's violet	" " "	" "	5	.3%	" "	" "	(-)		1630	1948
3533	Isamine blue *(C.I.No.710 is 6B or 8B: with .075-.15 gm neosalvarsan)*	Misc.car.	Man	2;2	5-20 ml	Repeated	iv	(+);(+)		1662	1923
3534	---- ---- (8588,in glycol or olive oil)	Car.;tr.tum.	Man;mouse	—	500;10	"	ip	(±);(+)		1663	1924
3535	---- ---- (68)	Sp.ma.car.	Mouse, Inbred	2	2	19-41	iv,sc	(-)		1664	1925
3536	" "	" " "	Mouse, Marsh	1	2	31	" "	(-)		1795	1926
3537	" "	Car., rectal	Man	1	10-20 ml	2	iv			1306	1927
3538	---- ---- (sometimes other medication)	Misc.car.	"	40	25-160	24(2-3ser.)	"	(+)(-)	Tox.	88	1928
3539	" "	" "	"	33	5-20 ml	24(2-3ser.)	"	5(+),8(-)	(+)	180	1928
3540	---- ---- (also eosin and PbS)	" "	"	8	5-20 ml	24(2-3ser.)	"	(+)	10(+)	181, 184	1928
3541	---- ---- (containing 2% glycerine)	Car., skin	"	5	5-20 ml	Daily-3day int.	"	(+)	(+)	181, 184	1928
3542	" "	Tr.:sar.;car., sar.	Rabbit; rat	—	1%	Daily int.	Inj.	(-)		1007	1928
3543	" "	Car.:breast;gast.	Man	1;1	5-20 ml	Daily-weekly	It,iv	(+);(+)		1038	1928
3544	---- ---- (8789T:± irrad.:± PbI_2 in sodium lactate)	Misc.car.	"	200	5-15 ml.5%	Daily, 1day int.	iv	(+),(-)	(+),(-)	1666	1929
3545	---- ---- (followed by irrad.)	" "	"	8	20-80	10-12/ser.	"	(+)	(+)	182, 183	1930
3546	---- ---- (68, alone: stabilized by glycerine)	Epithel.	"	2	25-100	9-16/ser.	"	(-)	(+)	407	1930
3547	---- ---- (8731,pure)	Tr.car.	Mouse	—	1-3	5 day int.	"	(+)		533	1930
3548	---- ---- (with gas treat.)	" "	"	—	2-3	5 day int.	"	(+)		640	1930
3549	---- ---- (with saccharated Fe_2O_3 or $FeSO_4(NH_4)_2SO_4$	" "	"	—	1-3	5 day int.	"	(±)		640	1930
3550	---- ---- (---- ---- ---- ---- and gas treat.)	" "	"	—	2-3	5 day int.	"	(+)		640	1930
3551	---- ---- (with $K_4Fe(CN)_6$ or $FeSO_4$)	" "	"	—	1-3	5 day int.	"	(-)		640	1930
3552	---- ---- in 2% serum albumin)	" "	"	—	1-3	—	—			640	1930
3553	" "	Tr.:F.J.car.;sar.	Rat;mouse	—	—	—	Inj.	(-)	Tox.	640	1930
3554	---- ---- (medicinal, with Bi)	Misc.car.	Man	109	30-100 ml	Repeated	iv	(+),13(-)	(+)	2086	1930
3555	" "	Ind.(tar)car.	Mouse	30-50	5	Weekly	"	(-)		2190, 2192	1930
3556	---- ---- (followed by irrad.)	Car., epithel.	Man	>1	40-160	2-3 day int.	"	--	(+)	659	1931
										1088	1931